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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/273,098 03/19/99 TESSIER-LAVIGNE M UC97-244-2

HM22/0502

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EXAMINER

ALLEN, M

ART UNIT	PAPER NUMBER
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1631

DATE MAILED:

05/02/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/273,098

Applicant(s)

Tessier-Lavigne et al.

Examiner
Marianne P. Allen

Group Art Unit
1631



- ☐ Responsive to communication(s) filed on _____
- ☐ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1035 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

- ☒ Claim(s) 1-11 _____ is/are pending in the application.
- Of the above, claim(s) 5, 10, and 11 _____ is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 1-4 and 6-9 _____ is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claims _____ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) _____.
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

- ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- ☒ Notice of References Cited, PTO-892
- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s) _____
- ☐ Interview Summary, PTO-413
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-4 and 6-9, drawn to Slit-N polypeptides and pharmaceutical compositions, classified in at least class 530, subclass 350, for example.
- II. Claim 5, drawn to the polynucleotide encoding Slit-N, classified in class 536, subclass 23.5.
- III. Claim 10, drawn to a method of promoting axon branching, classified in at least class 435, subclass 325, for example.
- IV. Claim 11, drawn to a method of treating neuropathy, classified in at least class 514, subclass 12, for example.

The inventions are distinct, each from the other because:

Inventions I and (III and IV) are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the products can be used in at least the two distinct claimed processes as well as to make antibodies.

Inventions I and II are structurally distinct products which can be shown to be distinct because they do not rely upon each other for their ultimate use and they require non-coextensive literature searches.

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The methods of Inventions III and IV do not require the polynucleotide of Invention II and thus Invention II can be considered distinct from these methods.

Inventions III and IV are distinct methods with different starting materials, method steps, and/or goals. They do not rely upon each other for their ultimate use and they require non-coextensive literature searches

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and the necessity for non-coextensive literature searches, restriction for examination purposes as indicated is proper.

During a telephone conversation with Mr. Richard Osman on 17 March 2000 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-4 and 6-9.

Affirmation of this election must be made by applicant in responding to this Office action. Claims 5 and 10-11 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

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Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78).

Presently, the first sentence of the specification contains incomplete information and does not appear to reflect that the prior application is a provisional application.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4 and 6-7 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,046,015. Although the conflicting claims are not identical, they are not patentably distinct from each other because they both claim isolated fragments of slit polypeptides. It would have been obvious and routine

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for one of ordinary skill in the art to make a composition of the polypeptide with a pharmaceutically acceptable excipient.

Claims 1-4 and 6-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to Slit-N polypeptides and pharmaceutical compositions thereof. The specification states that Slit-N polypeptides are proteolytic fragments of Slit proteins which stimulate elongation and branching of neuronal axons (page 2, lines 9-10). The specification states that Slit-N polypeptides encompass N-terminal fragments of Slit proteins which promote axon branching (page 3, lines 2-3). Note that these two disclosures are inconsistent with respect to providing a clear definition by structure and/or function for the broad class of proteins. Furthermore, the specification does not make clear what distinguishes an N-terminal fragment from other fragments of the protein. That is, it cannot be determined if a Slit-N polypeptide can be an internal fragment somewhere near the beginning of the Slit protein or if it can be any fragment as long as the first and neighboring contiguous amino acids are present (i.e. a fragment of amino acids 1-X where X is not the last amino acid). It does appear from the terminology that applicant means to exclude the naturally occurring, full length protein. It is unclear how this is to

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be interpreted with respect to any leader sequence or prosequence (the preproprotein) that may exist. That is, would the mature sequence meet the definition of a Slit-N polypeptide?

Although the specification states that Slit proteins are an art-recognized class of neuroactive proteins (page 3, lines 3-4), it provides no sequence information for any Slit or Slit-N polypeptide. Although Tables 1 and 2 describe mutants and give ranges of amino acids on page 4, these are without reference to a known base sequence. Although the specification refers to mammalian and human Slit-1-N, Slit-2-N, and Slit-3-N proteins, no particular sequences are provided or identified. Note that the Kidd et al., Brose et al., Wang et al., and Lit et al. references cited on page 2 of the specification do not appear to contain any sequence information. The specification provides no clear and limiting structural or functional definition to establish the metes and bounds of what constitutes an isolated Slit or Slit-N polypeptide.

In view of these facts, the specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). The skilled artisan cannot envision any of the contemplated proteins by a detailed chemical structure from the disclosure in the specification. There is a lack of written description for the broad genus (Slit-N polypeptide of claims 1, 3-4, 6, and 8-9) and subgenus (Slit-1-N, Slit-2-N, and Slit-3-N polypeptide of claims 2 and 7) of proteins claimed.

As none of the polypeptides are adequately described, they cannot be enabled because one would not know what to make. Applicant is also reminded that reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The enablement of the claims

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can be viewed similarly to those in Ex parte Maizel, 27 USPQ2d 1662, 1665. The Board of Patent Appeals and Interferences held that claims drawn to DNA sequences encoding biologically equivalent proteins (i.e. DNA encoding proteins that do not have a defined amino acid sequence) are not enabled when the specification discloses a single specific DNA sequence known to the inventor having the biological limitations.

Claims 2-3 and 6-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2 and 7 are indefinite for failing to have a terminal period (“.”).

Claim 3 is confusing in reciting “contained in a pharmaceutical composition.” It appears that applicant may have intended to claim a composition comprising the polypeptide of claim 1 and a pharmaceutically acceptable excipient; however, the claim language does not make this clear. Furthermore, the limitation “pharmaceutical composition” implies an intended use and/or a therapeutic amount for such an intended use which are not presently limitations in the claim.

Claims 6-9 are directed to pharmaceutical compositions and recite “therapeutically effective amounts.” However, no specific condition to be treated is recited in the claim and as such it cannot be determined what amounts of polypeptides the claims encompass. Claims 8-9 also fail to indicate the desired therapeutic effect or amount of the other neuroactive agent or NGF required.

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

Claims 1-4 and 6-7 are rejected under 35 U.S.C. 102(e) as being anticipated by Artavanis-Tsakonas et al. (U.S. Patent No. 5,789,195).

In view of the lack of a specific definition for a Slit-N polypeptide as set forth above, the claims have been interpreted as follows for the purposes of art. Itoh et al. (Molecular Brain Research, 1998) describes a Drosophila Slit gene as encoding a putative secreted protein which has leucine-rich repeats and epidermal growth factor (EGF)-like motifs and mammalian gene (human and rat) homologues with similar motifs. The expression patterns vary and the specific functions in Drosophila and mammals are unknown. (See abstract.) Nakayama et al. (Genomics, 1998) discloses identification of two mammalian homologues to a Drosophila Slit gene. The main characteristics disclosed are large size and presence of EGF-like domains. (See abstract and introduction.) The expression patterns of the homologues varied. (See pages 30-31, bridging paragraph.) The examiner did not identify any reference that provided an art recognized definition or limiting definition by structure and/or function as to what one of ordinary skill in the art would identify as a slit protein. In view of the specification's disclosures and the disclosure of these prior art references, the human notch EGF repeat fragment disclosed by Artavanis-

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Tsakonas et al. (see at least claims 15 and 74) would appear to be encompassed by the claims as the notch protein is involved in outgrowth of embryonic neurons and pathfinding (see column 4, lines 9-20), possesses EGF-like repeats, and is of large size. The isolated polypeptide fragments of containing EGF-like repeats are disclosed to be useful in pharmaceutical compositions to at least make antibodies (see columns 20-21). In the absence of a specific structure being associated with the designation hSlit-1-N, hSlit-2-N, and/or hSlit-3-N in the claims, the human polypeptide fragment of Artavanis-Tsakonas et al. anticipates these claims as well.

Claims 1-4 and 6-8 are rejected under 35 U.S.C. 102(e) as being anticipated by Goodman et al. (U.S. Patent No. 6,046,015).

Goodman et al. discloses human Slit-1 polypeptide fragments and pharmaceutical compositions thereof. Compositions containing collagen fibers are deemed to meet the limitation of another neuroactive agent as such fibers would have been routinely used to provide a substrate for neuronal growth. (See abstract; claims; column 4, lines 30-65; column 17, lines 5-50.)

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen, whose telephone number is (703) 308-0666. The examiner can normally be reached on Monday-Friday from 9:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028. Official FAX communications may be directed to either (703) 308-4242 or (703) 305-3014.

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Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Marianne P. Allen
MARIANNE P. ALLEN
PRIMARY EXAMINER
~~GROUP 1000~~
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